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EXAMINER	
KELLY, ROBERT M	
ART UNIT	PAPER NUMBER
1633	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/735,601	SMITH ET AL.	
	Examiner	Art Unit	
	ROBERT M. KELLY	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 July 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16 and 20-33* is/are pending in the application.

4a) Of the above claim(s) *1-15 and 20-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16,32 and 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: http://wiki.answers.com/Q/Amount_of_Genes_in_a_human_cell.

DETAILED ACTION

Applicant's amendment and argument of 7/24/09 are entered.

Claim 16 is amended.

Claim 33 is newly added.

Claims 1-16 and 20-33 are presently pending.

Election/Restrictions

Claims 1-15 and 20-31 remain withdrawn as drawn to non-elected inventions.

Claims 16, 32, and 33 are presently considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 16, 32, and 33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 16 requires the "full range" of antigens to be expressed. Claim 33 requires that the ARP preparation of Claim 16 be a subtractive expression library. These two claims, claimed with 33 being dependent, and emphasized by the term "full range" makes clear that the metes and bounds of "full range" are undefined. Does this mean all antigens? If so, then it would have appeared that Claim 16 is incorrectly dependent, however, the Examiner must give full credit to Applicant's claiming. Therefore, it must be that "full range" does not mean all antigens of the

tumor. The next question is then what does it mean, if it does not mean all antigens? Does it a representative group of antigens? If so, then the Art rejections below are proper, and the dependency is proper, because the subtractive hybrid would necessarily yield a representative group. If it were taken that the broad claim is meaning all antigens, then Claim 33 could not be interpreted to be properly dependent. Hence, for purposes of compact prosecution, the dependency is considered proper and the scope of full range is given the broadest reasonable interpretation: that of "a representative grouping of antigens". However, even though the claims are examined thusly, the claim still lacks clarity for its metes and bounds.

Claims 23 and 32 are rejected for depending from a rejected base claim and not overcoming the lack of clarity in such base claim. To wit, with regard to the limitation that directly addresses "full range", Claim 33, in stating "subtractive expression library" does not demonstrate what is to be subtracted, and hence, is still unclear for its metes and bounds; And Claim 32, depending from Claim 16, necessarily has the same problems with clarity.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting

ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 16, 32, and 33 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3-8, 10-15, 33-40, 44-49 and 51-77 of U.S. Patent No. 6,521,235 in view of Slovin, et al. (1999) Proc Natl Acad Sci, USA, 96(10): 5710-15, Nestle, et al. (1998) Nature Medicine, 4(3): 328-32, and Smooker, et al. (2000) Vaccine, 18: 2533-40, and Diatchenko, et al. (1999) Methods in Enzymology, 303: 349-380.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the differences between the inventions are the patent claiming specific viral replicons, claiming specific attenuating mutations, and the claiming of cancer antigen(s). However, the claims of the patent, do not claim specific antigens. However, the instant specification teaches attenuating mutations to the E1-E3 (e.g., p.6), and the specific attenuating mutations (the references cited in e.g., p. 6). Further, the patent teaches protozoa, bacterial, and viral antigens in general (e.g., cols. 5-6), but not tumor antigens. Lastly, subtractive hybridization is not taught to obtain a subset of antigens.

On the other hand, (i) Slovin teaches that multiple antigens for the tumor may be used to develop multivalent vaccines (e.g., ABSTRACT); (ii) Nestle teaches a cocktail of peptides used to produce cancer immunity (e.g., ABSTRACT), and (iii) Smooker demonstrates that a library of genes may be administered to develop an immune response. Lastly, Diatchenko teaches that

subtractive hybridization may be utilized to obtain the genes selectively expressed in a cancer (e.g., Example 4).

Hence, at the time of invention, it would have been obvious to modify the populations of VEE replicons of the patent to comprise multiple heterologous antigens from a tumor. The Artisan would do so to develop a multivalent vaccine and produce cancer immunity. The Artisan would also have a reasonable expectation of success, as such multivalent vaccines are already known to work.

Response to Argument – ODP 6,521,235

Applicant's argument of 7/24/09 has been fully considered but is not found persuasive.

Applicant argues that there is nothing about the salt-wash step, a tumor cell library, or a subtractive-hybridization library (pp. 9-10, paragraph bridging).

Such is not persuasive. The rejection is an obviousness-type double patenting rejection, based on the allowed claims of the patent, and subject matter already known by the Artisan, hence, to argue the Johnston patent alone is piecemeal argument and fails to recognize the knowledge within the Artisan's capability.

Applicant argues that salt wash step, related to the heparin binding ability of the derived particles, makes the claims allowable, by providing for much higher yields (pp. 10-11, paragraph bridging).

Such is not persuasive. Johnston teaches the particle manufacture, and Applicant has admitted on the record that Johnston teaches such particles (Interview Summary of 7/23/09), and hence, the particles claimed in Johnston necessarily are specifically encompassing the heparin binding particles. In fact, Applicant's presently-examined Application Specification teaches that

at least strain 3014 of VEE can bind heparin, in that it can be purified with heparin binding affinity chromatography (e.g., paragraph 0051), and Johnston teaches particles made with such mutations which allow the heparin binding (e.g., CLAIMS and EXAMPLES). Hence, the particles have the property of binding heparin. With regard to the salt-wash step, the composition is claimed, not the method of making, and the composition is not altered by the method of making within the claims. Applicant should claim the method of making if that is their invention, not the particles themselves, as such necessarily would yield patent-term extension for the Johnston patent.

With regard to the newly-claimed subtractive hybridization, Diatchenko teaches the use of such to obtain such antigens.

Claims 16, 32, and 33 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 32, 34-35, 37, 40, 42, 44-45, 47, 50-52, 54-55, 57, 60, 62, 64-65, 67, 70, 72, 74-75, 77, 80, 82, 84-90 of U.S. Patent No. 6,531,135 in view of Slovin, et al. (1999) Proc Natl Acad Sci, USA, 96(10): 5710-15, Nestle, et al. (1998) Nature Medicine, 4(3): 328-32, and Smooker, et al. (2000) Vaccine, 18: 2533-40, and Diatchenko, et al. (1999) Methods in Enzymology, 303: 349-380.

While the claims are not identical, the differences between the claims are the patent claiming specific virus replicons and the absence of tumor antigens in the patent . Further, the specifications each direct the artisan to use encoding sequences from similar viruses (e.g., PATENT, col. 5). However, the patent does not teach tumor antigens.

On the other hand, (i) Slovin teaches that multiple antigens for the tumor may be used to develop multivalent vaccines (e.g., ABSTRACT); (ii) Nestle teaches a cocktail of peptides used to produce cancer immunity (e.g., ABSTRACT), and (iii) Smooker demonstrates that a library of genes may be administered to develop an immune response. Lastly, Diatchenko teaches that subtractive hybridization may be utilized to obtain the genes selectively expressed in a cancer (whole article).

Hence, at the time of invention, it would have been obvious to modify the populations of VEE replicons of the patent to comprise multiple heterologous antigens from a tumor. The Artisan would do so to develop a multivalent vaccine and produce cancer immunity. The Artisan would also have a reasonable expectation of success, as such multivalent vaccines are already known to work.

Response to Argument – ODP 6,531,135

Applicant's response of 7/24/09 has been fully considered but is not found persuasive.

Applicant's arguments parallel the rejection against Johnston 6,521,235, above, and hence, the same response is given, as the patent here also teaches the VEE 3014 mutation.

Lastly, Diatchenko teaches that subtractive hybridization may be utilized to obtain the genes selectively expressed in a cancer (whole article).

Claims 16 and 32 remain rejected, and Claim 33 is newly rejected, on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 32, 34-35, 37, 40, 42, 44-45, 47, 50-52, 54-55, 57, 60, 62, 64-65, 67, 70, 72, 74-75, 77, 80, 82, 84-90 of U.S. Patent No. 6,156,558 in view of Slovin, et al. (1999) Proc Natl Acad Sci, USA, 96(10): 5710-15,

Nestle, et al. (1998) Nature Medicine, 4(3): 328-32, and Smooker, et al. (2000) Vaccine, 18: 2533-40, and Diatchenko, et al. (1999) Methods in Enzymology, 303: 349-380.

The differences between the instant claims and the patent claims are that the patent encompasses not only claims the generic alphavirus, but also claims specific viruses encompassed, and further comprises specific attenuating mutations. Moreover, the patent, while not specifically claiming antigens, does teach the use of viral antigens (e.g., col. 5).

On the other hand, (i) Slovin teaches that multiple antigens for the tumor may be used to develop multivalent vaccines (e.g., ABSTRACT); (ii) Nestle teaches a cocktail of peptides used to produce cancer immunity (e.g., ABSTRACT), and (iii) Smooker demonstrates that a library of genes may be administered to develop an immune response. . Lastly, Diatchenko teaches that subtractive hybridization may be utilized to obtain the genes selectively expressed in a cancer (whole article).

Hence, at the time of invention, it would have been obvious to modify the populations of VEE replicons of the patent to comprise multiple heterologous antigens from a tumor. The Artisan would do so to develop a multivalent vaccine and produce cancer immunity. The Artisan would also have a reasonable expectation of success, as such multivalent vaccines are already known to work.

Response to Argument – ODP against 6,156,558

Applicant's response of 7/24/09 has been fully considered but is not found persuasive.

Applicant's arguments parallel that applied to the Johnston Patents, above, and hence, the same answers are given.

. Lastly, Diatchenko teaches that subtractive hybridization may be utilized to obtain the genes selectively expressed in a cancer (whole article).

Claims 16, 32, and 33 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 22-26, 28-29, 31-34, and 36-37 of U.S. Patent No. 6,541,010 in view of Slovin, et al. (1999) Proc Natl Acad Sci, USA, 96(10): 5710-15, Nestle, et al. (1998) Nature Medicine, 4(3): 328-32, and Smooker, et al. (2000) Vaccine, 18: 2533-40 and Diatchenko, et al. (1999) Methods in Enzymology, 303: 349-380.

The differences between the instant claims and the patent's claims are that the patent has attenuating mutations encompassed, specific viruses encompassed, and no specific heterologous sequence claimed. However, the patent's specification teaches prokaryotic, eukaryotic, protozoa, and viral antigens (e.g., cols. 11-12, paragraph bridging), but no cancer anitgens.

On the other hand, (i) Slovin teaches that multiple antigens for the tumor may be used to develop multivalent vaccines (e.g., ABSTRACT); (ii) Nestle teaches a cocktail of peptides used to produce cancer immunity (e.g., ABSTRACT), and (iii) Smooker demonstrates that a library of genes may be administered to develop an immune response. Lastly, Diatchenko teaches that subtractive hybridization may be utilized to obtain the genes selectively expressed in a cancer (e.g., whole article).

Hence, at the time of invention, it would have been obvious to modify the populations of VEE replicons of the patent to comprise multiple heterologous antigens from a tumor. The Artisan would do so to develop a multivalent vaccine and produce cancer immunity. The Artisan

would also have a reasonable expectation of success, as such multivalent vaccines are already known to work.

Response to Argument – ODP against 6,541,010

Applicant's argument of 7/24/09 has been fully considered but is not found persuasive.

Applicant's arguments parallel the arguments given for the Johnston patents, above, and the same responses are given.

. Lastly, Diatchenko teaches that subtractive hybridization may be utilized to obtain the genes selectively expressed in a cancer (e.g., Example 4).

It is noted for the record that Applications 10/517,083 and 10/929,234, are abandoned, and hence, no ODP rejections are proper.

Claims 16 and 31 remain and/or are newly provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 20-22 and 28 of copending Application No. 11/132,711. Although the conflicting claims are not identical, they are not patentably distinct from each other because while the other Application's claims are drawn to replicons containing TC-83 structural proteins, and do not claim any particular heterologous sequences, the present specification teaches the use of TC-83 strain (which is VEE), because of its naturally attenuated phenotype (e.g., p. 17), and the other Application teaches all the same specifically claimed species of antigen (e.g., p. 25), and moreover TC-38 may be purified by heparin affinity chromatography (e.g., paragraph 24), and moreover Claims that it may be optimized, to comprise a number of immunogens from, e.g., a tumor (e.g.,

paragraph 0071 of the Application Publication 2005/0266550). Hence, in light of the teachings and claims of the 11/132,711 Application, it would have been obvious to make the present invention. The Artisan would have been motivated to do so in order to treat cancers. Moreover, the Artisan would have expected success, as the other Application teaches it will work.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Argument – ODP against 11/132,711

Applicant's argument of 7/24/09 has been fully considered but is not found persuasive.

Applicant appears to wish the rejections remain in abeyance, and hence, they are (e.g., pp. 12-13, paragraph bridging).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 16, 32, and 33 remain, or are newly, rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,156,558 to Johnston, et al., Patented 12/5/00, Nestle, et al. (1998) Nature Medicine, 4(3): 328-32 (ABSTRACT ONLY), and Smooker, et al. (2000) Vaccine, 18: 2533-40, for reasons of record, as further modified by Diatchenko, et al. (1999) Methods in Enzymology, 303: 349-380.

Johnston teaches the use of similar VEE and alpha-virus replicon particles, in vaccines. (E.g., ABSTRACT; col. 3, paragraph 4; col. 4, paragraph 2; cols. 7-8, paragraph bridging.) Moreover, Johnston demonstrates that the particles are sufficient to produce immune responses against foreign gene encoded proteins (e.g., FIGURE 3). However, Johnston does not teach a plurality of replicons encoding a plurality of antigens, or the use of antigens to cancer. Moreover, Johnston teaches making of particles with VEE 4031 structural proteins, which are taught to bind heparin.

On the other hand, Nestle teaches a cocktail of peptides used to produce cancer immunity (e.g., ABSTRACT), and Smooker demonstrates that a library of genes may be administered to develop an immune response. Moreover, Diatchenko teaches that subtractive hybridization may be utilized to obtain just those genes which are selectively expressed (whole article), and thereby necessarily also teaches expressing all the genes of the tumor.

Hence, at the time of invention, it would have been obvious to make a plurality of alphaviral replicons encoding the different peptides of Nestle. The Artisan would have been motivated to do so to produce an immune response to cancer, using the method of Smooker instead of actual delivery of the polypeptides. Moreover, the Artisan would have had a reasonable expectation of success, as Smooker had demonstrated that a plurality of antigens could have been so-delivered and Nestle teaches that the plurality of peptides produced immune response to cancer.

Response to Argument – 103, Johnston `558, Smooker, Nestle, Diatchenko

Applicant's argument of 7/24/09 has been fully considered but is not found persuasive.

Applicant argues that the salt-wash step provides for a much more efficient yield of viral particles that allow for more easily obtaining the rare members of the library and hence, the claim is allowable over the art cited (pp. 15-16, paragraph bridging).

Such is not persuasive. First, the rare members are in no way known to be preferentially-associated with the envelope, and hence, they could be obtained. Moreover, with regard to obtaining a sampling with the various antigens, it is clear that larger amounts of virus would simply need to be prepared, and there is nothing in the Art to demonstrate that larger volumes would not be possible to be grown. Lastly, the improvement is clearly commensurate with the method of production, but Applicant has claimed the particles themselves; improved methods of making do not change the structure of the composition, unless they truly change the structure of the composition obtained: such is not found here.

Applicant argues that yields in the patent are in the range of 3E5 to 1E8, while the present invention yields 10E10-10E11, and hence, rare genes could be found, while they would not be captured in the old process (p. 16, paragraph 2).

Such is not persuasive. First, even the yield of 1E8 more than covers finding rare genes, as it appears, for example, in the case of humans, current thought is that about 3E5 genes are expressed per body cell (http://wiki.answers.com/Q/Amount_of_Genes_in_a_human_cell). Hence, the Argument to finding rare members appears to be contradicted. Second, the yields of particles the patent are not the yields which can be obtained with larger cultures. Third, there is nothing to say that the rare genes are preferentially associated with the cell membrane such that the old methods of isolation would not yield those genes. Fourth, the method of making does not

make the composition patentable, unless it changes the structure of the composition from that of the Art.

Applicant argues that the patent "appears" to be limited to antigens related to Marburg virus, while the present application relates to a wide variety of antigen sources (p. 16, last paragraph).

Such is not persuasive. The patent claims all sorts of alphavirus replicons (e.g., Claim 1), the patent even claims VEE (e.g., Claim 2), and teaches strain 4031 (e.g., Figure 1). The present claims are in no way limited to Marburg and Claim VEE (Claims 16 and 32). With regard to the antigen sources, this is a rejection for obviousness, and hence, brings into consideration, on top of the other art cited, what the artisan understands, and hence, the rejection is proper. Just because Johnston may have failed to state that multiple virus particles contain distinct antigens does not mean that the Artisan could not Apply the knowledge in the Art to it, to thereby obtain equivalent structure. If Applicant is arguing for a specific interpretation of the claims, the claims are given their broadest reasonable interpretation, and not an argued-for interpretation.

Applicant argues something with regard to "paragraph 5 in col. 7" (pp. 16-17, paragraph bridging), but the Examiner is unable to determine what is being referred to, the patent or the present application, or one of the pieces of other art utilized, and hence, no answer is provided directly, except to say that Marburg does not appear to limit the rejection made.

Applicant argues that Smooker teaches small peptides, and hence, is a different approach taken than the present specification and claims (p. 17, paragraph 2).

Such is not persuasive. Smooker teaches obtaining the antigens, the claims are not limited to full-protein size antigens, and there is nothing to argue that the antigens would not be

obtained. Again, efficiency is not of issue, the claimed composition is. Still further, the rejection is one of obviousness, and the Artisan is aware that protein sequences must be context to be properly expressed and produce a proper antigen. Further, due to the amendments, in yet another interpretation, the inclusion of Diatchenko makes clear that it was known to obtain the cDNAs and as well as to further perform subtractive hybridization to obtain a second library. The inclusion of such libraries into vectors for vaccination is provided by the other art supplied. Lastly, piecemeal argument neglects the understanding of the Artisan and the other Art supplied.

Applicant argues that Nestly is drawn to vaccination of melanoma patients with peptide or tumor lysate pulsed dendritic cells, but doe snot teach a tumor cell expression library (p. 17, paragraph 3).

Such is not persuasive. As in the above piecemeal argument to Smooker, these references are simply not read in a vacuum, but in the context of the skill in the Art and the other art supplied. The rejection as supplied is correctly applied.

Applicant argues that only hindsight could anticipate the claims (pp. 17-18, paragraph bridging).

Such is not persuasive. Applicant's specification is not referenced in the rejection, except in arguments to show the same virus particles are taught by Johnston, and Applicant has claimed the composition, and the method of making does not change the structure obtained. Applicant's invention is one of a method of making, not a composition.

Claims 16, 32, and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,866,553 to Donnelly, et al., Patented 2/2/99, U.S. Patent No. 6,156,558 to

Johnston, et al., Patented 12/5/00 and Smooker, et al. (2000) Vaccine, 18: 2533-40, for reason of record, and as further considering Diatchenko, et al. (1999) Methods in Enzymology, 303: 349-380.

Donnelly teaches eliciting immune responses to papilloma virus via DNA constructs encoding papilloma virus gene products (e.g., ABSTRACT, TITLE). Further, several antigens are taught for such encoded genes, which may be used in combination (e.g. col. 5, paragraph 2). Still further, it is noted that papilloma virus is not only a virus, but a major cause of cancer in women (cervical cancer), and hence, such immunization is also against cancer.

Johnston teaches the use of the equivalent alpha-viral and VEE replicon particles, in vaccines. (E.g., ABSTRACT; col. 3, paragraph 4; col. 4, paragraph 2; cols. 7-8, paragraph bridging.) Moreover, Johnston demonstrates that the particles are sufficient to produce immune responses against foreign gene encoded proteins (e.g., FIGURE 3). Diatchenko teaches obtaining libraries of cells, and performing subtractive hybridization to find differentially-expressed genes (whole article).

Smooker teaches a library of epitopes, expressed on separate plasmids (a library), for immunizing mice against Plasmodium chabaudi, a protozoan (ABSTRACT). Diatchenko teaches obtaining libraries of cells, and performing subtractive hybridization to find differentially-expressed genes (whole article).

Hence, at the time of invention, it would have been obvious to modify the composition of Donnelly to encode different antigens of HPV in the alphaviruses of Johnston. The Artisan would have been motivated to do so to provide immunity against the virus HPV and cancer. Moreover, the Artisan would have had reasonable expectation of success, as Smooker had taught

that large libraries of particles could elicit immunity. Lastly, as these antigens are expressed in the papilloma-caused tumor cells, it is the equivalent of an expression library of such a tumor cell.

Response to Argument – 103, Donnelly/Johnston/Smooker/Diatchenko

Applicant's argument of 7/24/09 has been fully considered but is not found persuasive.

Applicant argues he recovery had by their method, which would require larger volumes to be used in the Art (pp. 18-19, paragraph bridging).

Such is not persuasive. The method of making does not exclude the fact that the Artisan could still make the same product prior to their invention, which is commensurate with an improved process of making, not the product obtained.

Applicant argues that Donnelly teaches at most 2 antigens, and hence, does not teach the multi-valent vaccines of the present invention (p. 19, last paragraph).

Such is not persuasive. The 2 antigens represent the full range of antigens of the cancer, given the broadest reasonable interpretation of "full range".

Applicant argues that Johnston does not teach the method of obtaining (p. 19, last paragraph).

Such is not persuasive. The composition is claimed, and the method of isolation does not alter the structure of the composition obtained. Applicant cannot have a patent to a composition, when the invention is the method of making.

Applicant argues hindsight reconstruction (p. 19, last paragraph).

Such is not persuasive. At best, the only hindsight reconstruction is to note that Johnston teaches a VEE that is heparin binding, and such is not hindsight reconstruction, but simply

demonstrating the VEE to be the same strain as what Applicant utilizes to demonstrate their invention.

Applicant argues that Smooker teaches biolistic particles, not alphavirus (pp. 19-21, paragraph bridging).

Such is not persuasive. The use of vectors is known in the Art, and Smook is not utilized for that part of the teaching, but simply expressing epitopes of antigens.

Applicant argues the improvement had by utilizing their method of preparation, and argues that such secondary considerations overcome the 103 rejection (p. 20, paragraph 2).

Such is not persuasive. The method of making does not make the already obvious composition allowable. Applicant should claim their invention in terms of their advancement in the Art.

Conclusion

No Claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT M. KELLY whose telephone number is (571)272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Robert M Kelly/
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